In The Claims

Please cancel claims 1-25 without prejudice.

Please add claims 26-45.

1-25 (CANCELLED)

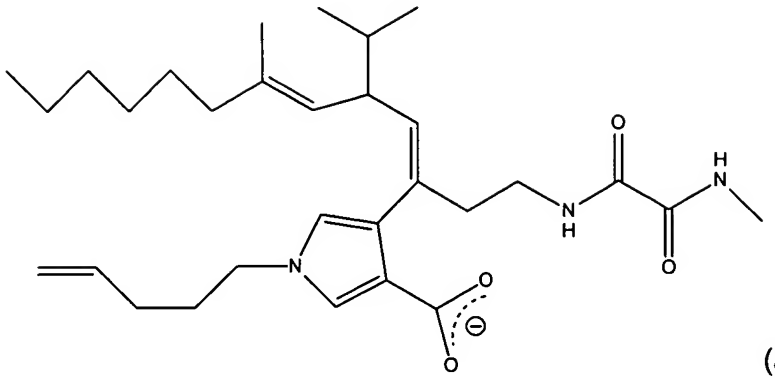
26 (ADDED) A method for the treatment of metabolic diseases in a mammal comprising co-administration to said mammal of (i) a compound capable of binding to a secondary binding site of DPIV and DPIV like enzymes and (ii) at least one anti-diabetic agent.

27 (ADDED) A method for the treatment of metabolic diseases in a mammal comprising co-administration to said mammal of (i) a compound capable of binding to a secondary binding site of DPIV and DPIV like enzymes and (ii) at least one anti-diabetic agent selected from the group consisting of:

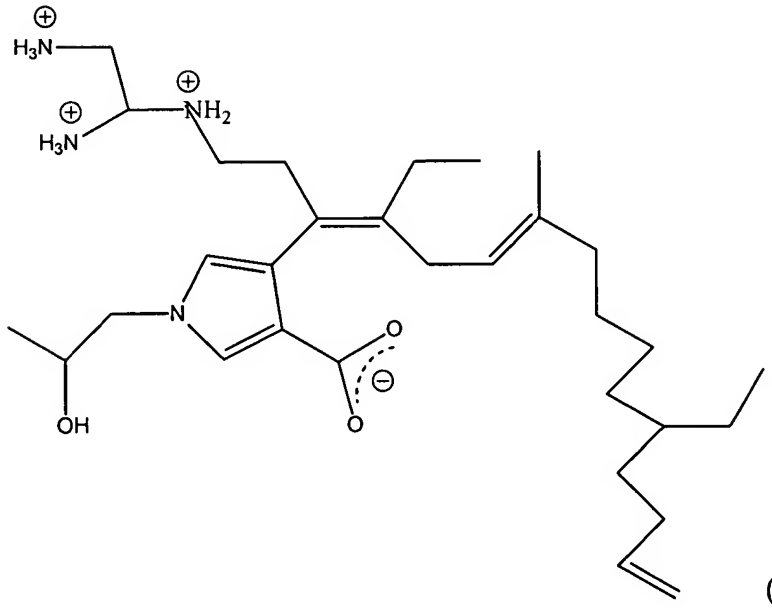
- DPIV inhibitors;
- PPAR agonists;
- biguanides, e.g. metformin, phenformin or buformin;
- protein tyrosin phosphatase-1B (PTP-1B) inhibitors;
- insulin and insulin mimetics;
- sulfonylureas and other insulin secretagogues;
- α-glucosidase inhibitors or acarbose;
- glucagon receptor agonists;
- GLP-1, GLP-1 mimetics, and GLP-1 receptor agonists;
- GLP-2, GLP-2 mimetics, and GLP-2 receptor agonists or teduglutide;
- exendin-4, exendin-4 mimetics, exenatide;
- GIP, GIP mimetics, and GIP receptor agonists;
- PACAP, PACAP mimetics, and PACAP receptor 3 agonists;

- PYY, PYY mimetics, PYY receptor agonists, and PYY receptor antagonists;
- one or more cholesterol lowering agents selected from the group consisting of:
    - HMG-CoA reductase inhibitors,
    - sequestrants,
    - nicotinyl alkohol, nicotinic acid and salts thereof,
    - PPARα agonists,
    - PPARγ agonists,
    - PPARα/γ dual agonists,
    - inhibitors of cholesterol absorption,
    - acyl CoA:cholesterol acyltransferase inhibitors, and
    - antioxidants;
- PPARδ agonists;
- anti-obesity compounds;
- an ileal bile acid transporter inhibitor; and
- anti-inflammatory agents.

28. (ADDED) The treatment method according to claim 27 wherein the compound is selected from the group comprising: a consensus sequence of the GRF-peptide family, TFTSDY, TFTDDY, H-Ser-D-Glu-Thr-Gly-D-Val-D-Lys-D-Val-OH, and compounds of formulas a) to d):



(a)



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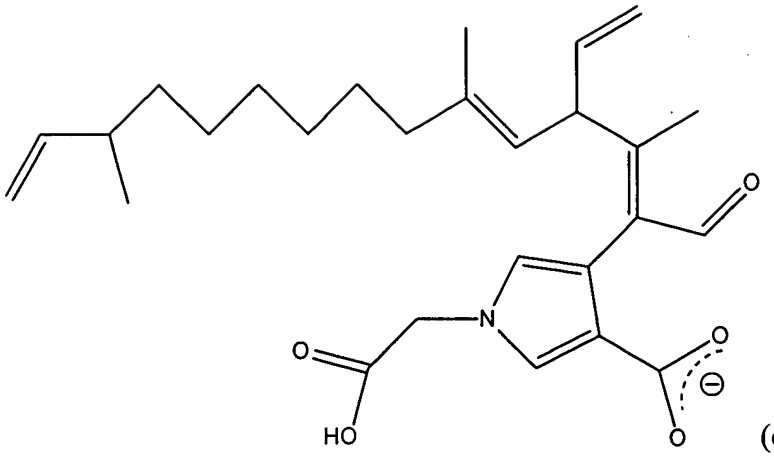
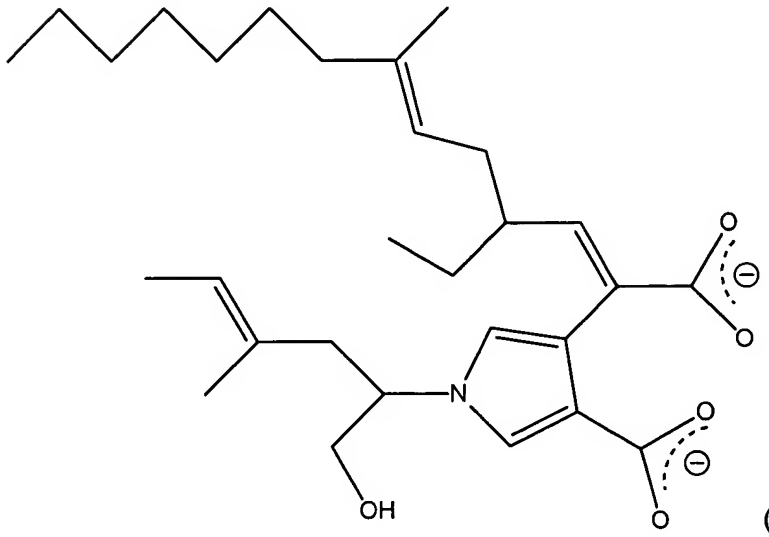


(c)



(d).

29. (ADDED) The treatment method according to claim 27 wherein the anti-diabetic agent is selected from DPIV inhibitors, metformin, exenatide, exendin-4, acarbose, insulin, and sulfonylureas.

30. (ADDED) The treatment method according to claim 27 wherein the metabolic disease is selected from Syndrome X, impaired glucose tolerance, glucosuria, lipid disorders, dyslipidemia, hyperlipidemia, hypertriglyceridemia, hypercholesterolemia, low HDL levels, high LDL levels, metabolic acidosis, hyperglycemia, diabetes mellitus, diabetic neuropathy and nephropathy and of sequelae caused by diabetes mellitus in mammals, metabolism-related hypertension and cardiovascular sequelae caused by hypertension in mammals.

31. (ADDED) The treatment method according to claim 27 for the prophylaxis and/or treatment of skin diseases, diseases of the mucosa, autoimmune diseases, inflammatory conditions, psychosomatic, neuropsychiatric and depressive illnesses, such as anxiety, depression, sleep disorders, chronic fatigue, schizophrenia, epilepsy, nutritional disorders, spasm and chronic pain, atherosclerosis and its sequelae, vascular restenosis, irritable bowel syndrome, inflammatory bowel disease, including Crohn's disease and ulcerative colitis, other inflammatory conditions, pancreatitis, abdominal obesity, neurodegenerative disease, retinopathy, nephropathy, ovarian hyperandrogenism (polycystic ovarian syndrome), growth hormone deficiency, neutropenia, tumor metastasis, benign prostatic hypertrophy, gingivitis, osteoporosis, and other conditions.

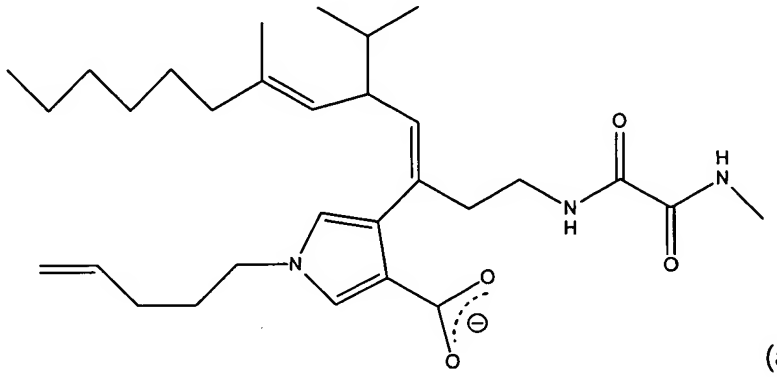
32. (ADDED) A pharmaceutical composition comprising a compound capable of binding to a secondary binding site of DPIV and DPIV like enzymes, at least one anti-diabetic agent and a pharmaceutically acceptable carrier therefore.

33. (ADDED) The pharmaceutical composition of claim 32 wherein said at least one anti-diabetic agent is selected from the group consisting of:

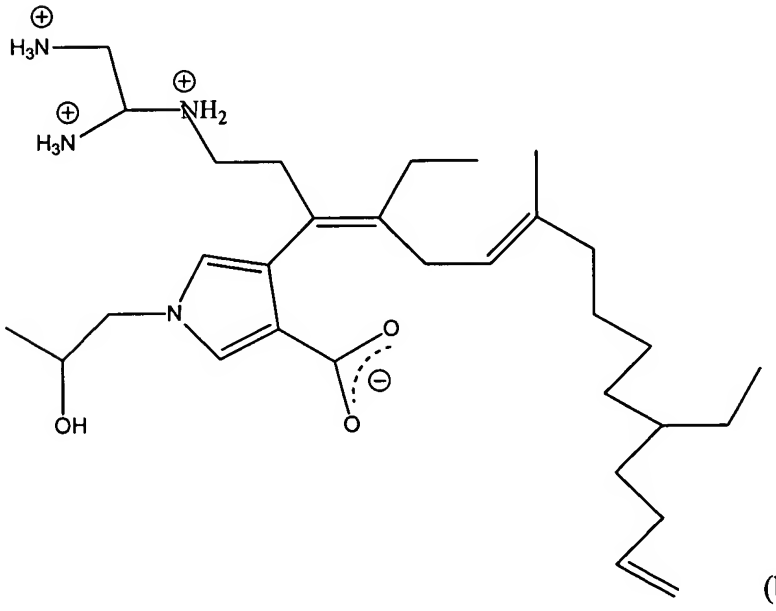
- DPIV inhibitors;
- PPAR agonists;
- biguanides, e.g. metformin, phenformin or buformin;
- protein tyrosin phosphatase-1B (PTP-1B) inhibitors;
- insulin and insulin mimetics;

- sulfonylureas and other insulin secretagogues;
- α-glucosidase inhibitors, acarbose;
- glucagon receptor agonists;
- GLP-1, GLP-1 mimetics, and GLP-1 receptor agonists;
- GLP-2, GLP-2 mimetics, GLP-2 receptor agonists, and teduglutide;
- exendin-4 and exendin-4 mimetics, and exenatide;
- GIP, GIP mimetics, and GIP receptor agonists;
- PACAP, PACAP mimetics, and PACAP receptor 3 agonists;
- PYY, PYY mimetics, PYY receptor agonists, and PYY receptor antagonists;
- cholesterol lowering agents selected from the group consisting of
    - HMG-CoA reductase inhibitors,
    - sequestrants,
    - nicotinyl alkohol, nicotinic acid and salts thereof,
    - PPARα agonists,
    - PPARγ agonists,
    - PPARα/γ dual agonists,
    - inhibitors of cholesterol absorption,
    - acyl CoA:cholesterol acyltransferase inhibitors, and
    - antioxidants;
- PPARδ agonists;
- antiobesity compounds;
- an ileal bile acid transporter inhibitor; and
- anti-inflammatory agents.

34. (ADDED) The pharmaceutical composition of claim 32 wherein the compound is selected from the group comprising: a consensus sequence of the GRF-peptide family, TFTSDY, TFTDDY, H-Ser-D-Glu-Thr-Gly-D-Val-D-Lys-D-Val-OH, and compounds of formulas a) to d):



(a)



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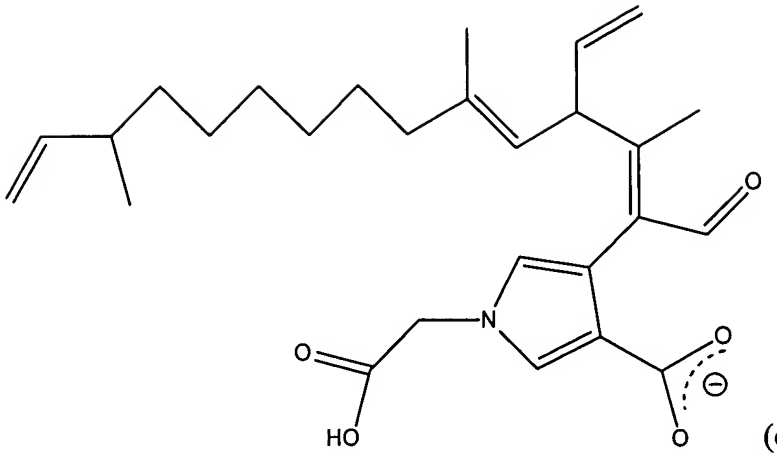

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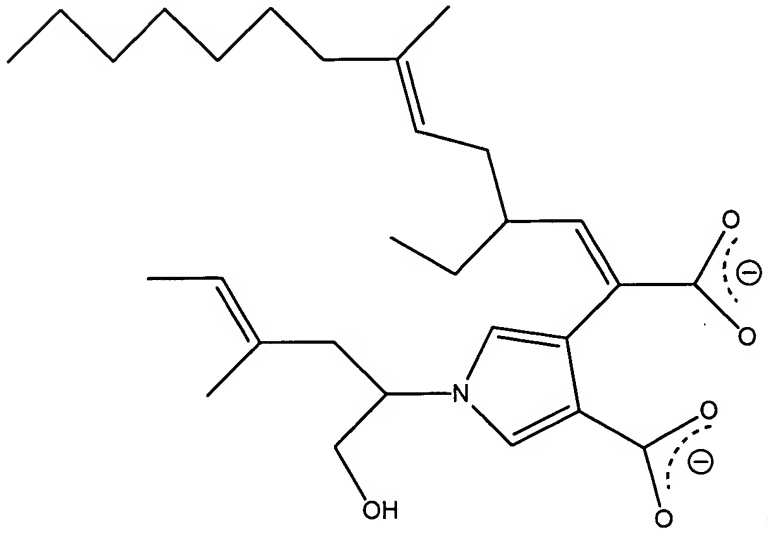

(d).

35. (ADDED) The pharmaceutical composition of claim 32 wherein said compound is TFTSDY or TFTDDY.

36. (ADDED) The pharmaceutical composition of claim 32 wherein said compound is H-Ser-D-Glu-Thr-Gly-D-Val-D-Lys-D-Val-OH.

37. (ADDED) The pharmaceutical composition of claim 32 wherein said compound capable of binding to a secondary binding site of DPIV and/or DPIV-like enzymes modulates the selectivity and/or activity of DPIV or DPIV-like enzymes in a mammal.

38. (ADDED) The pharmaceutical composition of claim 32 wherein said compound capable of binding to a secondary binding site of DPIV and/or DPIV-like enzymes substantially prevents of the interaction of DPIV or DPIV-like enzymes with their binding proteins in a mammal.

39. (ADDED) The pharmaceutical composition of claim 32 wherein said secondary binding site of DPIV and DPIV like enzymes comprises the amino acid residues L90, E91, T152, W154, W157, R310, Y330, R318, Y416, S460, K463, E464 and R560 of DPIV.

40. (ADDED) The pharmaceutical composition of claim 32 wherein said secondary binding site of DPIV and DPIV like enzymes comprises the amino acid residues Glu361 and Ile407 and Nε2 of His363 of DPIV.

41. (ADDED) The treatment method according to claim 27 wherein the compound blocks the product release site of DPIV and/or DPIV-like enzymes.

42. (ADDED) The treatment method according to claim 27 wherein the compound substantially prevents the tetramerization of DPIV and/or DPIV-like enzymes.

43. (ADDED) The treatment method according to claim 27 wherein the compound comprises 3 to 20 amino acid residues.

44. (ADDED) The treatment method according to claim 27 wherein the compound comprises 5 to 12 amino acid residues.

45. (ADDED) The treatment method according to claim 27 wherein the compound comprises 5 to 7 amino acid residues.